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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/676,135	09/29/2000	Bryan J. Boyle	21272-034	9596

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EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	10

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/676,135	Applicant(s) BOYLE ET AL.	
	Examiner Jehanne Souaya	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13,24,25 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13,24,25 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group II, claims 10-13 and 25, SEQ ID NO 4 in Paper No. 9 is acknowledged. The response states that applicants reserve the right of rejoinder of Group VI, claim 24 and Group VIII, claim 29 upon the allowance of the product claims. Applicant is reminded with regard to claim 24, that the claims rejoined must be commensurate in scope with any claims allowed. With regard to claim 29, should the product claims be found allowable after the issuance of a final rejection, prosecution would be reopened to include a rejection under 35 USC 112/1st paragraph for the methods of treatment of claim 29.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Applicant's claim for priority to applications 09/560,875, filed 4/27/2000, and 09/496,914, filed 2/3/2000, is acknowledged. However, the currently pending claims, 10-13, and 25, have not been awarded the benefit of the earlier filing date of either application as the subject matter in the claims is not disclosed in either the '875 or the '914 applications.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 101

Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the specific and substantial tests (see below).

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. ' 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility."

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a specific or substantial utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. ' 101. This analysis should, or

course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial asserted utility would be considered to be met.

A "Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.
See also the MPEP at 2107 - 2107.02.

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 10-13 and 25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims encompass isolated polypeptides that are at least 98 % identical to SEQ ID NOS 4 and have metallocarboxypeptidase like activity. The claims further encompass the mature protein of SEQ ID NO 4. The specification defines "mature protein coding region" (p. 19) as a polypeptide lacking a signal sequence. Since the specification teaches that amino acids 1-20 of SEQ ID NO 4 are drawn to a signal peptide, the recitation of "mature protein thereof" in claim 10 is interpreted to mean a polypeptide comprising amino acids 21-374 of SEQ ID NO 4. The claims further encompass a polypeptide which hybridizes to the protein coding portion of SEQ ID NO 4 under a set of specified conditions. It is noted that SEQ ID NO 4 is drawn to an amino

acid sequence. The claim has been interpreted, therefore to encompass the recitation of SEQ ID NO 3, which is drawn to the nucleic acid sequence that encodes SEQ ID NO 4.

The specification teaches that SEQ ID NO 4 is predicted to be encoded by the nucleic acid of SEQ ID NO 3, and that a signal peptide is predicted to be encoded by amino acids 1-20 of SEQ ID NO 4. The specification further teaches that a predicted fifteen residue GPI anchor exists at amino acids 360-374 of SEQ ID NO 4, and that predicted zinc binding regions as well as predicted carboxypeptidase A metalloprotease (M14) family signature domains were found throughout SEQ ID NO 4 (p.4). The specification, however, does not demonstrate the biological activity or function of SEQ ID NOS 4 or where "active domains" are located. Such a demonstration is critical for the artisan to know how to use SEQ ID NO 4 as carboxypeptidases that belong to the GPI anchor class, such as carboxypeptidase M, have different biological activity and substrate specificity (cleave basic amino acids and are involved in processing of peptide hormones) than that of carboxypeptidase A (cleaves hydrophobic amino acids from peptides in the gut– see Reznik and Fricker, Cell. Mol. Life Sci, 2001, pp 1790-1804, vol. 58, figure 1). The specification asserts that the signal peptide, has use on its own, but teaches that this use(which is not disclosed in the specification) must be confirmed by expression in mammalian cells and sequencing of the cleaved product.

Metallocarboxypeptidases are generally known to be involved in cleavage of peptides, however a large class of Metallocarboxypeptidases exist which have zinc binding regions and also have a wide range of functions (see Vendrell et al, Biochimica et Biophysica Acta; 2000;

vol. 177, pp 284-298), therefore the prediction of a putative GPI anchor region as well as zinc binding regions and putative carboxypeptidase A metalloprotease (M14) family signature domains in SEQ ID NO 4 would not indicate to one of skill a specific or substantial utility for the claimed polypeptides. Further, the specifications disclosure of a specific or substantial utility for the claimed polypeptide is unclear as the specification teaches that SEQ ID NO 4 also has homology to carboxypeptidase B, whose biological activity and function is different than that of carboxypeptidase A. It is further noted that the specification asserts at page 11, that SEQ ID NO 4 is expected to have either secreted metallocarboxypeptidase like activity (it is noted that Carboxypeptidase A and B, while having different functions, are considered part of the family of secreted carboxypeptidases) or GPI anchored metallocarboxypeptide like activity (it is noted that such carboxypeptidases belong to a different class of carboxypeptidases than that of carboxypeptidase A or B, which have different biological activities and functions than the latter, see Vendrell et al). Thus, given such conflicting teachings in the specification, one of skill would not know how to use the polypeptide of SEQ ID NO 4.

The specification asserts the following uses for the claimed polypeptides: at page 49, the specification teaches that the polypeptides can be used a) to generate an antibody that specifically binds the polypeptide, b) as molecular weight markers, and c) as food supplements. The specification further asserts that the claimed polypeptides can be used as potential therapeutics in digestive disorders, autoimmunity, inflammatory disorders and Alzheimer's disease (p. 14). At page 49, the specification teaches that the polypeptides can also be used in assays to determine

biological activity or levels of protein in biological fluids, and also to isolate correlative receptors or ligands. The claimed polypeptides, however, are not supported by a specific asserted utility because the disclosed uses of the polypeptides are not specific and are generally applicable to any polypeptide. These are non-specific uses that are applicable to polypeptides in general and not particular or specific to the polypeptide being claimed.

Further, the claimed polypeptides are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a polypeptide can be used to obtain an antibody. The antibody could then be used in conducting research to isolate the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case, none of the antibodies that are to be produced as final products resulting from processes involving the claimed polypeptides have specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported

by a specific and substantial asserted utility for the reasons set forth above, credibility of the utility has not been assessed.

It is noted that the specification teaches that SEQ ID NO 4 has about 46% identity to Bothrops jararaca carboxypeptidase homologue and 48% identity to mutant carboxypeptidase B. Neither the specification, nor the art teach the activity or biological function of Bothrops japonica carboxypeptidase homologue. Further, the art teaches the pitfall of using homology to assign protein function. Bork (TIG, vol. 12, pp 425-427) teaches that a single wrongly annotated entry will lead to whole families with artificial functions based on similarities to that entry (see p. 426, col 1) and that similarities might only be restricted to certain domains, but the function is transferred to a whole protein(col. 3). With respect to the % identity to carboxypeptidase B mutant, a sequence search revealed that SEQ ID NO 4 also has 39.6 % identity to bovine carboxypeptidase B (cleaves basic amino acids) as well as 38.1% identity to mouse carboxypeptidase A (cleaves hydrophobic amino acids). Further, Reznik teaches that carboxypeptidases which have different functions, but belong to the same subfamily, only have about 50% homology to each other. Therefore, absent any evidence as to the actual function or activity of the polypeptide of SEQ ID NO 4, one skilled in the art would not know whether the biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule. Further, with respect to claims 12 and 13, which are drawn to a polypeptide having a certain % identity or number of residues in common, it is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function

of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. (See Proudfoot et al, J. Biol. Chem., vol. 271 pp. 2599-2603 which teaches that in recombinant human RANTAS, a single residue at the amino terminus of the molecule can change the activity of the polypeptide, see abstract). The specification does not teach the biological function or activity of SEQ ID NO:4. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding utility. Further experimentation would be required of the skilled artisan to determine a use for the polypeptides of the claimed invention. As noted by Brenner v. Manson, 383 US 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use - testing... a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Claim Rejections - 35 USC § 112

Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 10-13 and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make or use the claimed invention.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See In re Wands, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

Quantity of Experimentation Necessary
Amount of Direction and Guidance
Presence and Absence of Working Examples
Nature of the Invention
Level of predictability and unpredictability in the art

It is noted that given the disclosure of the sequence of SEQ ID NO 4 in the specification, one of skill in the art would be enabled to make the polypeptide of SEQ ID NO 4. The skilled artisan, however, would not be enabled to use the polypeptide of SEQ ID NO 4, kits or compositions comprising such, nor would the skilled artisan be enabled for making or using variants or homologs of SEQ ID NO 4.

The claimed invention is drawn to a polypeptide of SEQ 4, or the mature protein thereof. The claimed invention is also drawn to an isolated polypeptide comprising an amino acid sequence which is at least 98% identical to SEQ ID NOS 4, and has metallocarboxypeptidase like activity, or encoded by a polynucleotide which hybridizes to the polynucleotide which encodes SEQ ID NO 4, under a specific set of conditions. The specification, however, does not define what activity is encompassed by the term "carboxypeptidase-like". With regard to the mature protein of SEQ ID NO 4, absent a teaching of a specific amino acid sequence that is "the mature protein" of SEQ ID NO 4, the examiner assumes that such is drawn to amino acids 21-364 of SEQ ID NO 4 as the specification defines "mature protein coding region" at p. 19 to be a polypeptide without a signal sequence and the specification also teaches that amino acids 1-20 of SEQ ID NO 4 correspond to a signal peptide.

The specification teaches the sequence of SEQ ID NO 4. The specification, however, does not teach one of skill in the art how to use the polypeptide of SEQ ID NO 4, nor the mature protein of SEQ ID NO 4 (amino acids 21-364 of SEQ ID NO 4). The specification teaches that SEQ ID NO 4 is predicted to be encoded by the nucleic acid of SEQ ID NO 3, and that a signal peptide is predicted to be encoded by amino acids 1-20 of SEQ ID NO 4. The specification further teaches that a predicted fifteen residue GPI anchor exists at amino acids 360-374 of SEQ ID NO 4, and that predicted zinc binding regions as well as predicted carboxypeptidase A metalloprotease (M14) family signature domains were found throughout SEQ ID NO 4 (p.4). The specification, however, does not demonstrate the biological activity or function of SEQ ID

NOS 4 or where "active domains" are located. Such a demonstration is critical for the skilled artisan to know how to use SEQ ID NO 4 as carboxypeptidases that belong to the GPI anchor class, such as carboxypeptidase M, have different biological activity and substrate specificity (cleave basic amino acids and are involved in processing of peptide hormones) than that of carboxypeptidase A (cleaves hydrophobic amino acids from peptides in the gut– see Reznik and Fricker, Cell. Mol. Life Sci, 2001, pp 1790-1804, vol. 58, figure 1). The specification asserts that the signal peptide, has use on its own, but teaches that this use (which is not disclosed in the specification) must be confirmed by expression in mammalian cells and sequencing of the cleaved product.

Metallocarboxypeptidases are generally known to be involved in cleavage of peptides, however a large class of metallocarboxypeptidases exist which have zinc binding regions and also have a wide range of functions (see Vendrell et al, Biochimica et Biophysica Acta; 2000; vol. 177, pp 284-298), therefore the prediction of a putative GPI anchor region as well as zinc binding regions and putative carboxypeptidase A metalloprotease (M14) family signature domains in SEQ ID NO 4 would not indicate to one of skill a specific or substantial utility for the claimed polypeptides. Further, the specifications disclosure of a specific or substantial utility for the claimed polypeptide is unclear as the specification teaches that SEQ ID NO 4 also has homology to carboxypeptidase B, whose biological activity and function is different than that of carboxypeptidase A. It is further noted that the specification asserts at page 11, that SEQ ID NO 4 is expected to have either secreted metallocarboxypeptidase like activity (it is noted that

Carboxypeptidase A and B, while having different functions, are considered part of the family of secreted carboxypeptidases) or GPI anchored metallocarboxypeptide like activity (it is noted that such carboxypeptidases belong to a different class of carboxypeptidases than that of carboxypeptidase A or B, which have different biological activities and functions than the latter, see Vendrell et al). Thus, given such conflicting teachings in the specification, one of skill would not know how to use the polypeptide of SEQ ID NO 4.

It is noted that the specification teaches that SEQ ID NO 4 has about 46% identity to Bothrops jararaca carboxypeptidase homolog and 48% identity to mutant carboxypeptidase B. Neither the specification, nor the art teach the activity or biological function of Bothrops japonica carboxypeptidase homolog. Further, the art teaches the pitfall of using homology to assign protein function. Bork (TIG, vol. 12, pp 425-427) teaches that a single wrongly annotated entry will lead to whole families with artificial functions based on similarities to that entry (see p. 426, col 1) and that similarities might only be restricted to certain domains, but the function is transferred to a whole protein(col. 3). With respect to the % identity to carboxypeptidase B mutant, a sequence search revealed that SEQ ID NO 4 also has 39.6 % identity to bovine carboxypeptidase B (cleaves basic amino acids) as well as 38.1% identity to mouse carboxypeptidase A (cleaves hydrophobic amino acids). Further, Reznik teaches that carboxypeptidases which have different functions, but belong to the same subfamily, only have about 50% homology to each other. Therefore, absent any evidence as to the actual function or activity of the polypeptide of SEQ ID NO 4, one skilled in the art would not know whether the

biochemical activity of the claimed subject matter would be the same as that of a similar known biomolecule.

Further, the claimed invention broadly encompasses active domains of the claimed polypeptides as well as variants, mutants, and homologs of the claimed polypeptides, with altered, or wildtype function or activity. It is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. (See Proudfoot et al, J. Biol. Chem., vol. 271, pp. 2599-2603 which teaches that in recombinant human RANTAS, a single residue at the amino terminus of the molecule can change the activity of the polypeptide, see abstract. The specification does not teach the biological function or activity of SEQ ID NO 4. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding enablement.

Since the specification has not demonstrated the function or biological activity of SEQ ID NO 4, and since the recitation of functionally different domains and the disclosed sequence similarity provides an unpredictable and unreliable correspondence between the activity of SEQ ID NO 4 and similar biomolecules, the skilled artisan would be required to perform undue experimentation to make or use the claimed polypeptides. As stated previously, the specification has not taught the function of the polypeptides of SEQ ID NO 4 nor has the specification taught

where to modify the polypeptide to produce a protein with at least 98% identity to SEQ ID NO 4, therefore, the skilled artisan would have no way of knowing which polypeptide sequences were responsible for the activity of the claimed polypeptides because the specification does not provide a description of the amino acid sequences which constitute these "active domains". The instant claims are drawn to undisclosed sequences encoding modifications that have not been contemplated. The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for it's activity. Due to the lack of guidance from the specification as to which parts of the claimed polypeptides correspond to active domains, these modifications and manipulations would require trial and error, which is considered undue experimentation. In addition, further experimentation would be required of the skilled artisan to determine a use for the polypeptides of the claimed invention.

Written Description

8. Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is based on a lack of written description.

he specification discloses SEQ ID NO: 4. Polypeptides comprising SEQ ID NOS 4 meet the written description provisions of 35 USC 112, first paragraph. However, claims 12 and 13

broadly encompass functional fragments, mutated sequences, allelic variants, and splice variants from any species. None of these sequences meet the written description provision of 35 USC 112, first paragraph since the specification provides insufficient written description to support the genus encompassed by the claim. The teachings of Reznik et al and Vellard et al illustrate that carboxypeptidases are a diverse class of proteins, and that proteins from this broad genus, while containing certain structural similarities to carboxypeptidases, have different functions. Thus a single sequence from this broad genus is not representative of the functionally different proteins from this broad class. Absent a written description disclosing a representative number of proteins of this broad class of carboxypeptidases, the specification fails to show that applicant was "in possession of the claimed invention" at the time the application for patent was filed. It is known for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. (See Proudfoot et al, J. Biol. Chem., vol. 271, pp. 2599-2603 which teaches that in recombinant human RANTAS, a single residue at the amino terminus of the molecule can change the activity of the polypeptide, see abstract). The specification does not teach the biological function or activity of SEQ ID NO 4, therefore, the disclosed structure of the sequence of SEQ ID NO 4 is not representative of the genus of polypeptides encompassed by the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS:4 , the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it

obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Accordingly, the specification does not provide a written description of the invention of claims 12 and 13.

Indefinite

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is indefinite as the claim recites "the polynucleotide of SEQ ID NO 4", however, SEQ ID NO 4 is directed to an amino acid sequence.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claim 13 is rejected under 35 U.S.C. 102(a) as being anticipated by Dumas Milne Edwards (hereinafter referred to as Dumas, EP1033401; Sept 6, 2000).

Dumas teaches a sequence (SEQ ID NO 452) which contains 313 out of 331 nucleic acids that are identical to the sequence of SEQ ID NO 3 from position 29 to position 341, which includes a portion of the protein coding region of SEQ ID NO 3 (alignment included, Accession number AAC00454). Thus, the sequence taught by Dumas, which encodes for a polypeptide of SEQ ID NO 4529 (see col. 19 and 20), would hybridize to the sequence of SEQ ID NO 3 under the conditions specified in the claims.

Conclusion

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Art Unit 1634

Jehanne Souaya
6/17/2002